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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,581	04/30/2002	Mortimer M. Civan	22253-67116 US	1751

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EXAMINER	
JAGOE, DONNA A	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 08/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,581	CIVAN ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,38-55,68,92 and 93* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,38-55,68,92 and 93* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/3/03&3/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 24 July 2004 has been entered.

The amendment filed 24 July 2004 has been received and entered. Claims 1, 68, 92 and 93 have been amended and claims 56-37 and 69-91 have been canceled.

Information Disclosure Statement

The information disclosure statement filed 23 March 2003 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. See documents 64-67 and 69-77. There is not copy of the cited documents provided. The remainder of the IDS has been considered.

Claims 1, 38-55, 68, 92 and 93 are pending.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 38-43, 47-55, 68, 92 and 93 are rejected under 35 U.S.C. 102(b) as being anticipated by Drug Facts and Comparisons (1994).

The claims are drawn to a method of regulating salt uptake or release by ciliary cells of a human eye or eye of an animal having a trabecular network by controlling or modulating the function of one or more antiports of aqueous humor ciliary epithelial cells by administering to the ciliary epithelial cells of the aqueous humor a modulating amount of a pharmaceutical composition consisting essentially of a modulator or one or more antiports. The antiports are Na^+/H^+ exchanger (the NHE-1 antiport) and a Cl^-/HCO_3^- exchanger (the AE2 antiport). Examples of the modulators beta blockers (particularly timolol), amilorides and cariporide

Drug Facts and Comparisons teach timolol, a beta blocker, to be employed to reduce elevated and normal intraocular pressure with or without glaucoma (page 2287). The mechanism appears to be a reduction of aqueous production, and a slight increase in outflow facility. Regarding claims to modulation of the antiports, this action is considered to be inherent. Applicants' attention is directed to *Ex parte Novitski*, 26 USPQ2d 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a *haec verba* recitation for such utility. In the instant application, as in Ex *parte Novitski*,

supra, the claims are directed to preventing a malady or disease with old and well-known compounds or compositions. It is now well-settled law that administering compounds inherently possessing a protective utility anticipates claims directed to such protective use. Arguments that such protective use is not set forth *haec verba* are not probative. Prior use for the same utility clearly anticipates such utility, absent limitations distancing the proffered claims from the inherent anticipated use. Attempts to distance claims from anticipated utilities with specification limitations will not be successful. At page 1391, *Ex parte Novitski*, supra, the Board said "We are mindful that, during the patent examination, pending claims must be interpreted as broadly as their terms reasonably allow. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). As often stated by the CCPA, "we will not read into claims in pending applications limitations from the specification." *In re Winkhaus*, 52 F.2d 637, 188 USPQ 219 (CCPA 1975)." In the instant application, Applicants' failure to distance the proffered claims from the anticipated **prophylactic** utility renders such claims anticipated by the prior inherent use.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 38-41, 44-45, 47-55, 68, 92 and 93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burke, U.S. Patent No. 5,215,991.

Burke teaches methods and pharmaceutical compositions of Na^+/H^+ exchange inhibitors which are employed to lower intraocular pressure (IOP) and for treatment of intraocular hypertension (increased intraocular pressure)(see abstract). Na^+/H^+ exchange inhibitors such as amiloride analogs improve the ocular hypotensive profile of various alpha 2 agonists when co-administered with the alpha 2 agonist (column 1, line 56 to column 2, line 5). It differs in that it does not teach glaucoma. It teaches

intraocular hypertension. Since both intraocular hypertension and glaucoma both result in increased intraocular pressure, it would have been obvious to administer amiloride to lower the intraocular pressure associated with glaucoma. Motivation to employ amiloride for glaucoma would come from the teachings of Burke that amiloride successfully treats intraocular pressure associated with intraocular hypertension.

Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Burke as applied to claims 1 and 1 and 38-41, 44-45, 47-55, 68, 92 and 93, and further in view of Scholz et al. U.S. Patent No. 6,348,476.

Burke teaches methods and pharmaceutical compositions of Na^+/H^+ exchange inhibitors which are employed to lower intraocular pressure (IOP) and for treatment of intraocular hypertension (increased intraocular pressure)(see abstract). Na^+/H^+ exchange inhibitors such as amiloride analogs improve the ocular hypotensive profile of various alpha 2 agonists when co-administered with the alpha 2 agonist (column 1, line 56 to column 2, line 5).

It does not teach cariporide.

Scholtz et al. teach that cariporide is a NHE inhibitor. It does not teach cariporide to lower intraocular pressure. Since Burke teaches Na^+/H^+ exchange inhibitors (NHE inhibitors) to lower intraocular pressure (IOP) it would have been obvious to employ cariporide to lower intraocular pressure associated. It would have been made obvious to one of ordinary skill in art at the time it was made to employ cariporide to lower intraocular pressure since Burke teaches inhibitors of NHE to lower intraocular pressure and Scholtz teaches that cariporide is an inhibitor of NHE. Such a modification would

have been motivated by the reasoned expectation of producing a composition, which is effective in comprehensively treating persons suffering from glaucoma.

Response to Arguments

Applicant asserts that the importance of the antiports in controlling the balance of fluid between secretion and outflow by the ciliary epithelial cells and the trabecular network was unknown until the present invention and the antiports control of salt balance in the aqueous humor could not be controlled in the antiports. The examiner differs. Applicant has merely found an explanation to what already occurs. The reduction of intraocular pressure in glaucoma when a beta-blocker such as timolol, cariporide or amilorides is applied. Further, applicant indicates that the composition is administered to the ciliary epithelial cells of the aqueous humor. There does not seem to be any description of how one would bypass administering an eyedrop to an eye to administer said compositions to the ciliary epithelial cells of the aqueous humor. A prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is **necessarily present**, or **inherent**, in the single anticipating reference. Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1268 (Fed. Cir. 1991). Other precedents of the court have held that inherent anticipation does not require that a person of ordinary skill in the art at the time would have recognized the inherent disclosure. E.g., *In re Cruciferous Sprout Litig.,* 301 F.3d 1343, 1351 (Fed. Cir. 2002); *Mehl/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1366 (Fed. Cir. 1999) ("Where the result is a *necessary consequence* of what was deliberately intended, it is of no import

that the article's authors did not appreciate the results."); Atlas Powder, 190 F.3d at 1348-49 ("Because 'sufficient aeration' was inherent in the prior art, it is irrelevant that the prior art did not recognize the key aspect of [the] invention. An inherent structure, composition, or function is not necessarily known."). In the instant case, the unappreciated anticipation also does not require recognition. Applicant claims to have discovered the method of modulating aqueous secretion by modulating the antiports of the aqueous humor. Since the pharmaceutical compositions claimed by applicant produced the claimed modulation of aqueous secretion, the discovery of the modulation of the antiport is inherent. In the context of the accidental anticipation, beta-blockers, such as timolol, do not accidentally modulate the antiport when the pharmaceutical composition is applied to a patient in need of treatment. The antiport necessarily and inevitably is modulated when the beta-blocker is applied and does not require a skilled artisan to recognize the inherent characteristic in the prior art that anticipates the claimed invention.

Applicant argues that Burke does not reduce intraocular pressure by the administration of the same agent as that of the instant invention. In response, "Products of identical chemical composition (i.e. cariporide) can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims (i.e. reduction of intraocular pressure) are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) (Applicant argued that the claimed composition was a pressure sensitive adhesive

containing a tacky polymer while the product of the reference was hard and abrasion resistant. "The Board correctly found that the virtual identity of monomers and procedures sufficed to support a prima facie case of unpatentability of Spada's polymer latexes for lack of novelty."). In other words, if cariporide alone did not lower intraocular pressure in Burke, it is not clear to the examiner how cariporide would lower intraocular pressure in the instant case. Knowledge of the movement of salt in the antiports would not give the same eyedrop administered by Burke the power to lower intraocular pressure by Civan et al.

Regarding applicants objections Scholtz et al., Scholtz et al. is combined with Burke et al. because Scholtz et al. teach that cariporide is a NHE inhibitor and Burke et al. teaches the utility of NHE inhibitors to lower intraocular pressure (IOP).

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Thursday from 9:00 A.M. - 3:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Donna Jagoe
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08/05/2005

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